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A PROGRESS REPORT ON RADIO TELEMETRY FROM INSIDE THE BODY

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ABSTRACT

Different units have been demonstrated that are small enough to fit in the eye, powerful enough to transmit from a freely swimming dolphin in ocean water, stable enough to transmit multiple information continuously for years after implanting, and suitable for tracking wild animals. Both laboratory and field experiments are described, using both passive and active transmitters.

INTRODUCTION

The telemetering of physiological information from within the body of man and animals has progressed far since its origin in 1952. At that time, I was interested in a problem in urology and asked one of my students, Mr. Bob Markevitch, to explore some possibilities for pressure transmission by radio from within the bladder. We were unable to power an active transmitter using one of the original point-contact transistors and so passive transmission was explored. Parts of his 1954 undergraduate research report to me are reproduced in Fig. 1. The development of junction transistors allowed active transmission, and the first generally available article on this subject (1), duly noting the previous work, was published with Jacobson, whom I had interested while working in Sweden. We named these ingestible units "endoradiosondes". At about that time, and since, workers in many parts of the world have contributed (2,3).

Some advances from my laboratory are indicated in the following figures, which will be discussed more fully in my lecture. Units can be made small enough to be surgically implanted in the front chamber of the eye in connection with the glaucoma problem (3), and others are powerful enough to telemeter from within an untethered dolphin (4). The wing motion of hummingbirds has been monitored from the voltages induced in a coil by a small section of magnetized needle on the wing, and the same could be done to monitor ear motion of the horseshoe bat. In humans, observations are routine, e.g., the testing of drugs is proving useful. In this case, localization is effected with the help of a trailing thread and the swallowing of barium before taking X-rays; if the thread is used to restrain motion onward by the capsule, then it is found that the gut will instead slide backwards and forwards somewhat over it.

I have also tracked and studied cold-blooded animals in the wild state; on the Galapagos Islands, I followed diurnal deep body temperature cycles in 400 pound tortoises and in the remarkable marine iguana.

New circuits that are more stable and longer lived have been developed. Units have been implanted and are still transmitting continuously after well over a year. A half-dozen different variables can simultaneously be transmitted from within a small animal. Even blood pressure can be monitored relatively well using the principle of the Mackay-Marg tonometer (5). Gastrointestinal bleeding site can be localized (3), but recent reports of boron toxicity suggest employing a different hydrogen peroxide reaction rather than using sodium perborate, even though the latter is used in tooth powder.

Plastics have been studied for their permeability properties. Both passive and active transmitter types are highly developed, and have different spheres of utility. New antenna types without coils are valuable, and both omnidirectional methods and booster transmitters have been brought to a satisfactory state. Various modulation methods have been explored, one of the most satisfactory being pulse-frequency modulation (1). Factors affecting the choice of the basic radio frequency are now better understood, the latter being chosen in a range from about 50 kilocycles to 100 megacycles, depending on application.

The following figures amplify on some of these matters. In these, it is assumed that the reader is familiar with at least reference 3; the serious worker is cautioned that fallacious surveys have recently appeared in otherwise reputable journals dealing with medical electronics.

ACKNOWLEDGMENT

For technical assistance, I would like to thank Harvey Fishman, Fred Jenkinson, Don Bukla, Ross McIntyre, Mark Bohrod, Barbara Dengler, and Ernie Woods. This work has been aided by NASA Grant # NSG 600

REFERENCES

(1) Mackay, R. S. and Jacobson, B., "Endoradiosonde", Nature, Vol. 179, p. 1239, June 15, 1957.

(2) Mackay, R. S., "Radio Telemetering from Within the Body", Science, Vol. 134, p. 1196, Oct. 20, 1961.

(3) Mackay, R. S., "Radio Telemetry from Inside the Body", New Scientist, Vol. 19, p. 650, Sept. 26, 1963.

(4) Mackay, R. S., "Deep Body Temperature of Untethered Dolphin Transmitted by Ingested Radio Transmitter", Science, scheduled May, 1964.

(5) Mackay, R. S., "The Application of Physical Transducers to Intracavity Pressure Measurement, with Special Reference to Tonometry", Medical Electronics & Biological Engineering Vol. 2, p. 3, Mar. 1964.

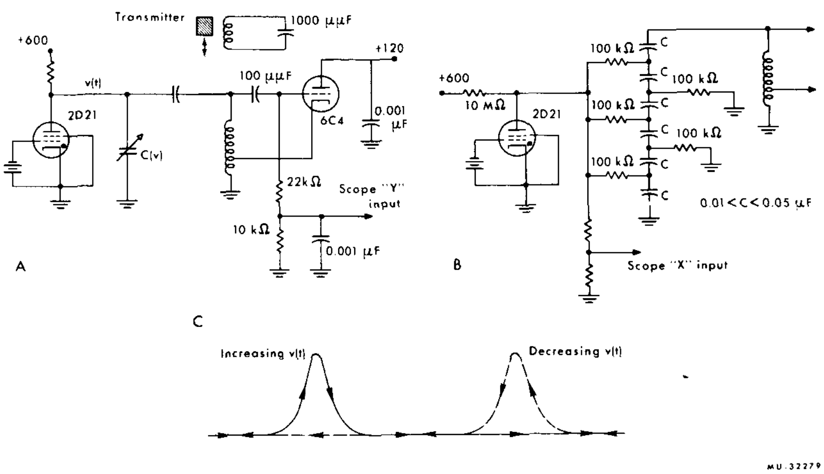

Fig. 1. Three figures from undergraduate research report by Bob Markevitch dated Summer, 1954, depicting the use of a scanning grid-dip meter to follow the output of an internal passive transmitter. This arrangement gave useful signals from within the mouth, but was not tested in the bladder. Some of these circuit methods are still valuable. (A): Connections for display of output on oscilloscope using a voltage sensitive condenser to provide the frequency sweep. (B): Placing several nonlinear condensers in series gives a linear effect in the meter circuit while leaving them in parallel and thus sensitive with regard to the control voltage. (C): Oscilloscope display; peaks shift with core motion.

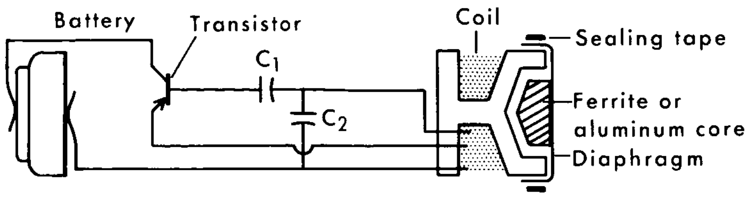

Fig. 2. Frequency modulated pressure sensing transmitter configuration based on the 1957 circuit (Ref. 1). Periodic blocking is observed in addition, with a frequency that depends on temperature if the transistor is of germanium. Better blocking action is obtained with a silicon transistor and a resistor from base to collector; if this resistance is small, continuous oscillation results. Variable R in the form of a thermistor or cadmium sulphide cell, or variable C_1 in the form of a pressure sensitive condenser fabricated of anodized aluminum sheets, can modulate the blocking frequency.

The continuously oscillating form is excellent for transmitting fluctuations such as peristaltic contractions, but when absolute pressures are to be determined over long periods, the following arrangements must be employed.

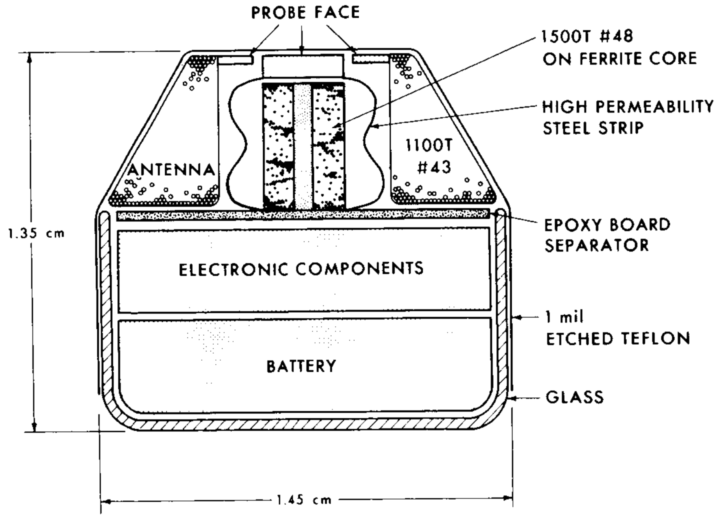

Fig. 3. Unit for continuously telemetering blood pressure through the intact blood vessel wall after clamping to an artery. The principle is that

Fig. 3. (continued) of a force transducer surrounded by an insensitive coplanar annulus, as in the Mackay-Marg tonometer. Animal experiments indicate that, if the readings are to be independent of the elastic properties of the blood vessel wall, and changes therein, then total motion of the transducer (degree of coplanarity) must be limited to less than 0.001 inch.

The battery case and antenna coil are separated for good radiation efficiency. A Hamilton watch battery #162171 will run such a unit for about two years; battery terminals are attached by spot welding. The correct antenna coil polarity must be used in the output stage. The teflon cover is glued into place; Kel F may be used if it proves less permeable to body fluids.

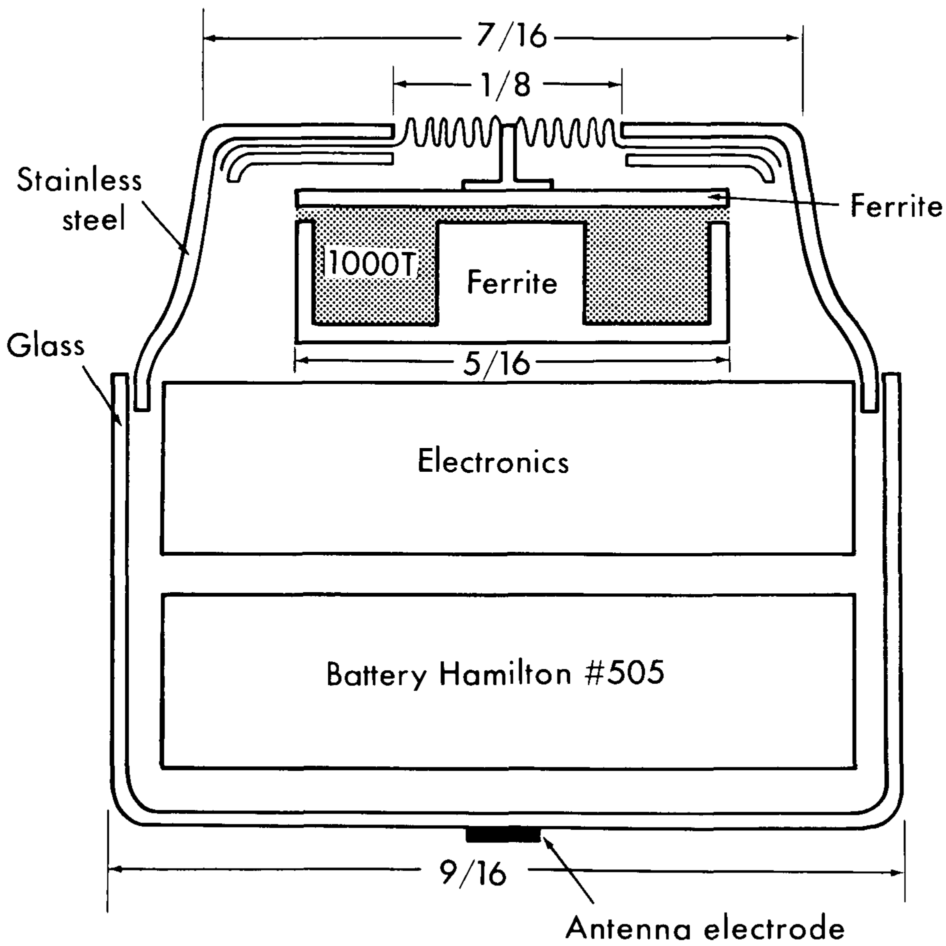

Fig. 4. Unit similar to above using stainless steel "bellows", more sensitive motion transducer, and a transmitting antenna consisting of two conducting electrodes contacting the body rather than a loop of wire (see Ref. 4). All dimensions are in inches. No materials permeable to body fluids are exposed.

Fig. 3. (continued) of a force transducer surrounded by an insensitive coplanar annulus, as in the Mackay-Marg tonometer. Animal experiments indicate that, if the readings are to be independent of the elastic properties of the blood vessel wall, and changes therein, then total motion of the transducer (degree of coplanarity) must be limited to less than 0.001 inch.

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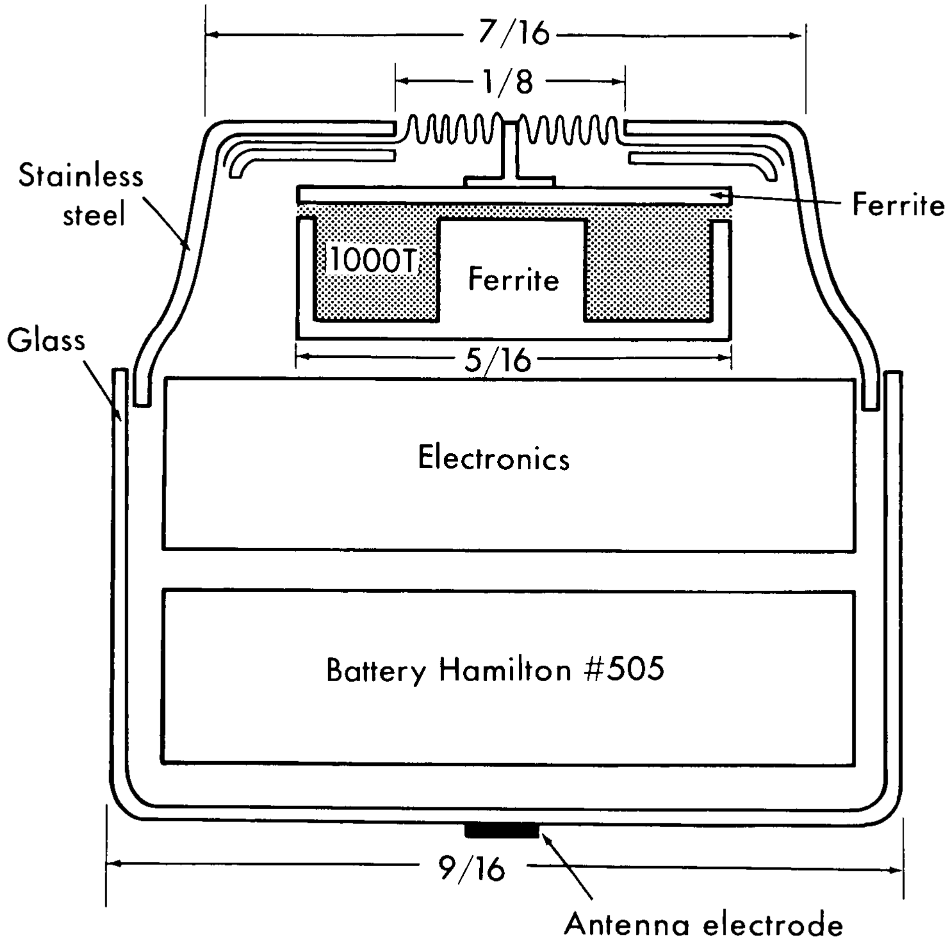


Fig. 4. Unit similar to above using stainless steel "bellows", more sensitive motion transducer, and a transmitting antenna consisting of two conducting electrodes contacting the body rather than a loop of wire (see Ref. 4). All dimensions are in inches. No materials permeable to body fluids are exposed.

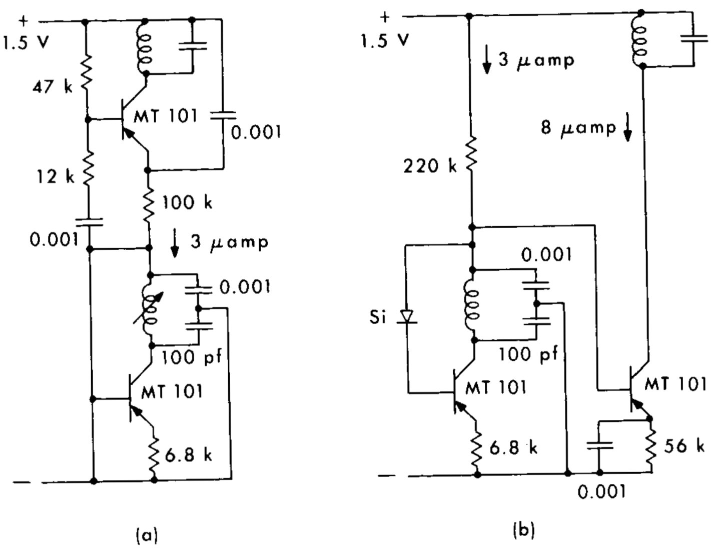


Fig. 5. Stable low current transmitters, each with a separate output stage. Part a: With three microamperes total current drain from a single battery cell, there is 0.6 volts peak-to-peak across the antenna coil at the top. Current drain can be further reduced by increasing the 100k resistor. Part b: With a total current drain of eleven microamperes, there is 1.8 volts across the antenna coil.

Stray capacity across the 6.8k resistor reduces the independence of these circuits on transistor properties. A single silver oxide cell is used for power. Frequency can be modulated by changing the 100 pf condenser rather than the inductance.

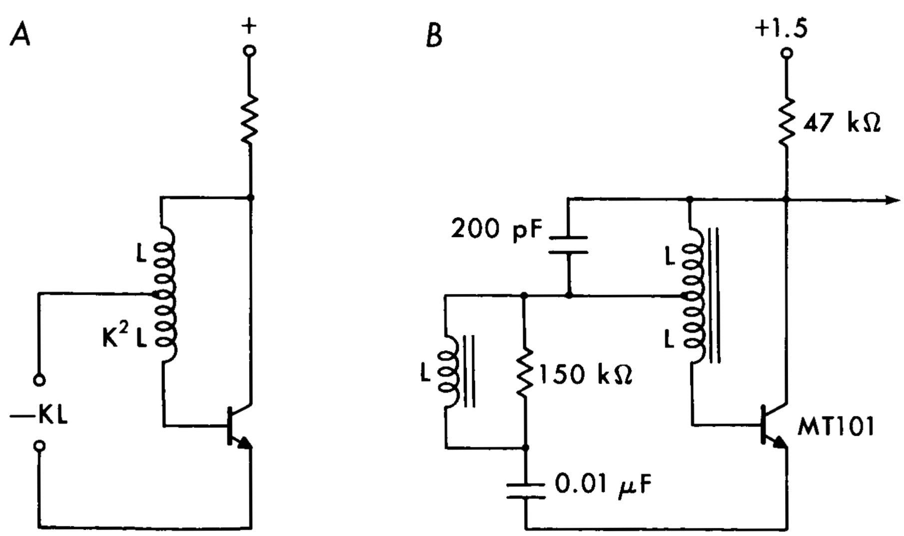


Fig. 6. A "negative impedance" can be used to cancel most of the unchanging impedance in a transducer, thus leaving any changes to produce larger percentage frequency shifts. (A) Negative inductance circuit. (B) Simplified oscillator; armature motion near one coil increases frequency and near other decreases it.

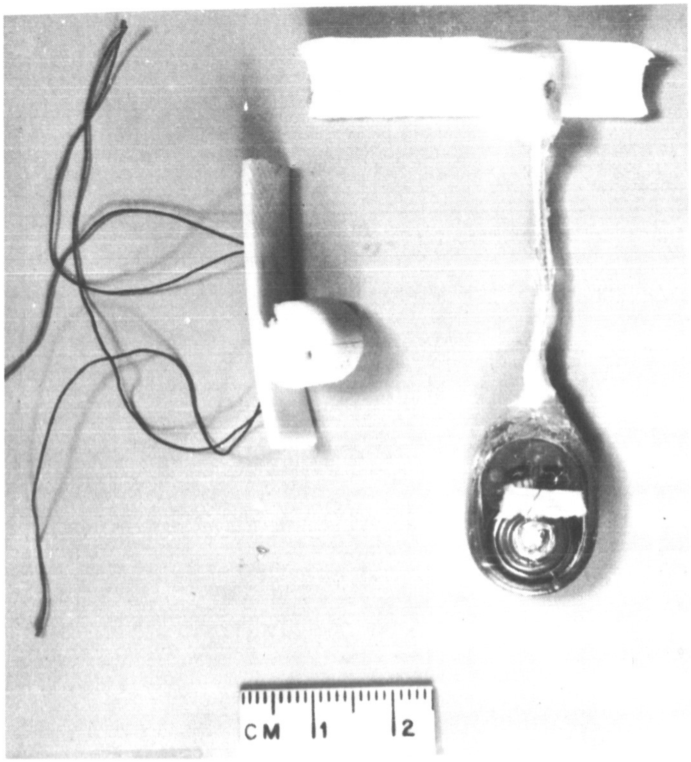


Fig. 7.

Supporting cuff for holding blood pressure transducer into contact with an artery, the unit shown separating the transducer and transmitter, the latter to be at a convenient subcutaneous position. The cuff is formed of Silastic 382 in a Teflon mold, with the thin part being cast over Dacron mesh. The artery is slipped into the notch seen in the left-hand unit, after which the extensions are wrapped around and tied. Such units have been in place for three months on the carotid artery of a dog and for a year on the aorta of a rabbit without causing damage.

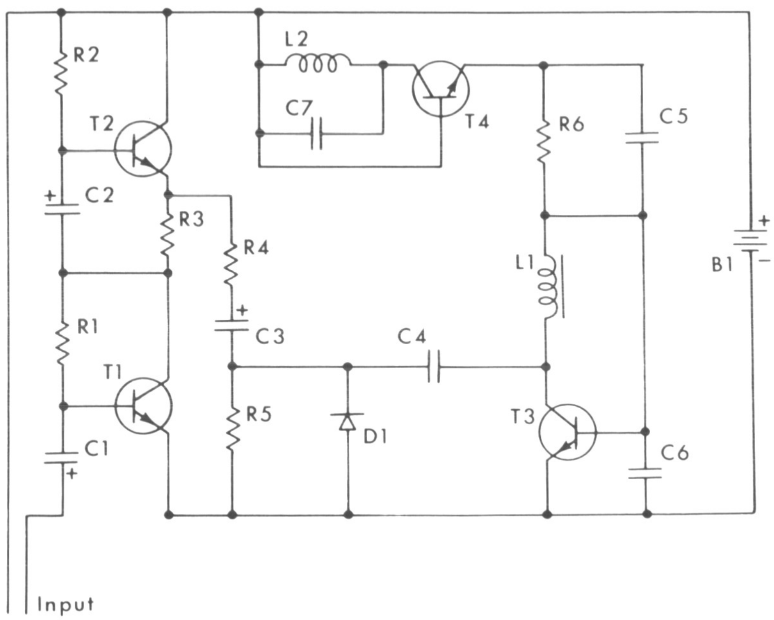


Fig. 8. Circuit that is frequency modulated by the action of the nonlinear diode D1 in response to electroencephalographic voltage changes. For electrocardiographic signals, one input stage of amplification can be omitted.

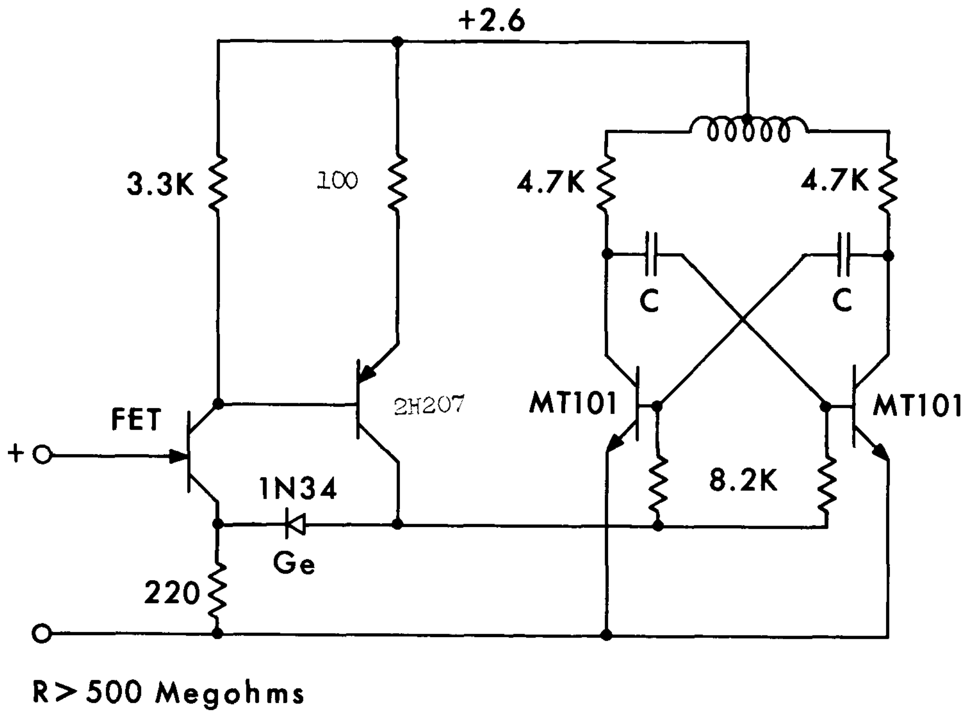


Fig. 9. High input resistance circuit suitable for accepting the signals from oxygen electrodes, pH electrodes, or glass electrodes for sensing other ions. The field-effect transistor was a Crystalonics C623. The diode temperature compensates the astable multivibrator, whose frequency range is set by choice of C. Larger frequency shifts are observed than with competing methods employing a nonlinear condenser.

WATER ABSORPTION OF EPOXY RESINS

Resin	Hardener	Resin/Hardener	14 Days	28 Days
Epon 826(1)	EM 308(2)	1/1	2.3%	3.6%
Epon 826	EM 308	2/1	1.0%	1.5%
Epon 826	Versamid 140(3)	1/1	1.9%	3.3%
Epon 826	Versamid 140	2/1	1.0%	1.6%
DER 332(4)	EM308	2/1	1.0%	1.3%
DER 332	Versamid 140	1/1	2.8%	4.5%
DER 332	Versamid 140	2/1	0.9%	1.5%
EC-2216 B(5)	EC-2216A	2/3	2.0%	2.8%
Armstrong A-2(6)	Activator E	100/6	1.0%	
Armstrong A-2	Activator A	100/4	0.9%	1.5%
Armstrong C-3	Activator E	100/12	3.9%	6.0%
Armstrong C-3	Activator A	100/8	1.2%	1.7%
Epocast 202(7)	D-40 (7)	100/15	2.0%	2.8%
Epocast 202	TETA (7)	10/1	0.9%	1.3%
Epocast 202	TETA	5/1	2.4%	3.5%
Epocast 202	DTA (8)	10/1	1.0%	1.6%
Epocast 202	DTA	5/1	5.9%	8.8%
Epocast 202	AEP (8)	10/1	1.0%	1.7%
Epocast 202	AEP	5/1	2.8%	3.9%
DER 332	AEP	100/15	1.0%	1.6%
DER 332	DTA	10/1	2.1%	3.2%
DER 332	Versamid 140	3/1	0.9%	1.3%
Silastic 382(10)			<.1%	
Type A Adhesive(10)			.2%	
Acrylic			0.9%	1.3%
Teflon(9)			<.1%	<.1%
Glass			<.1%	<.1%
Araldite 6005(11)	131H(11)136(11)	10/3/3	0.5%	0.7%
Araldite 6005	131H	2/1	0.5%	0.7%
Versalon 1112(3)			0.4%	
Versalon 1175(3)			0.7%	
Epocast 202	Versamid 140	7/3	1.3%	
Epocast 202	Versamid 115	7/3	1.1%	
Epon 826	Versamid 140	7/3	1.0%	
Epon 826	Versamid 115	7/3	1.2%	
Araldite 6005	Versamid 140	7/3	1.0%	
Araldite 502	TETA	100/8	.9%	
Epocast 202	TETA	100/6	.9%	

All epoxy resins were cured 7 days at 55-60 C. Cylinders of the plastic approximately 1 1/2 cm. diameter, 1 cm. length, were soaked in 0.9% saline at 39 C. (Numbers in parenthesis refer to manufacturers name.)

1. Shell Chemical Co.
2. Thiokol Chemical Corp.
3. General Mills
4. Dow Chemical Co.
5. 3-M Company
6. Armstrong Products
7. Furane Plastics
8. E. V. Roberts & Assoc.
9. E.I. DuPont Co.
10. Dow Corning
11. Ciba Products

Fig. 10. Most epoxy resins and other plastics are somewhat permeable to body fluids, and this can cause circuits contained therein to drift. Though perhaps not a specific criterion of excellence, these changes in weight upon soaking are suggestive. Silastic does not much slow absorption by underlying plastic.

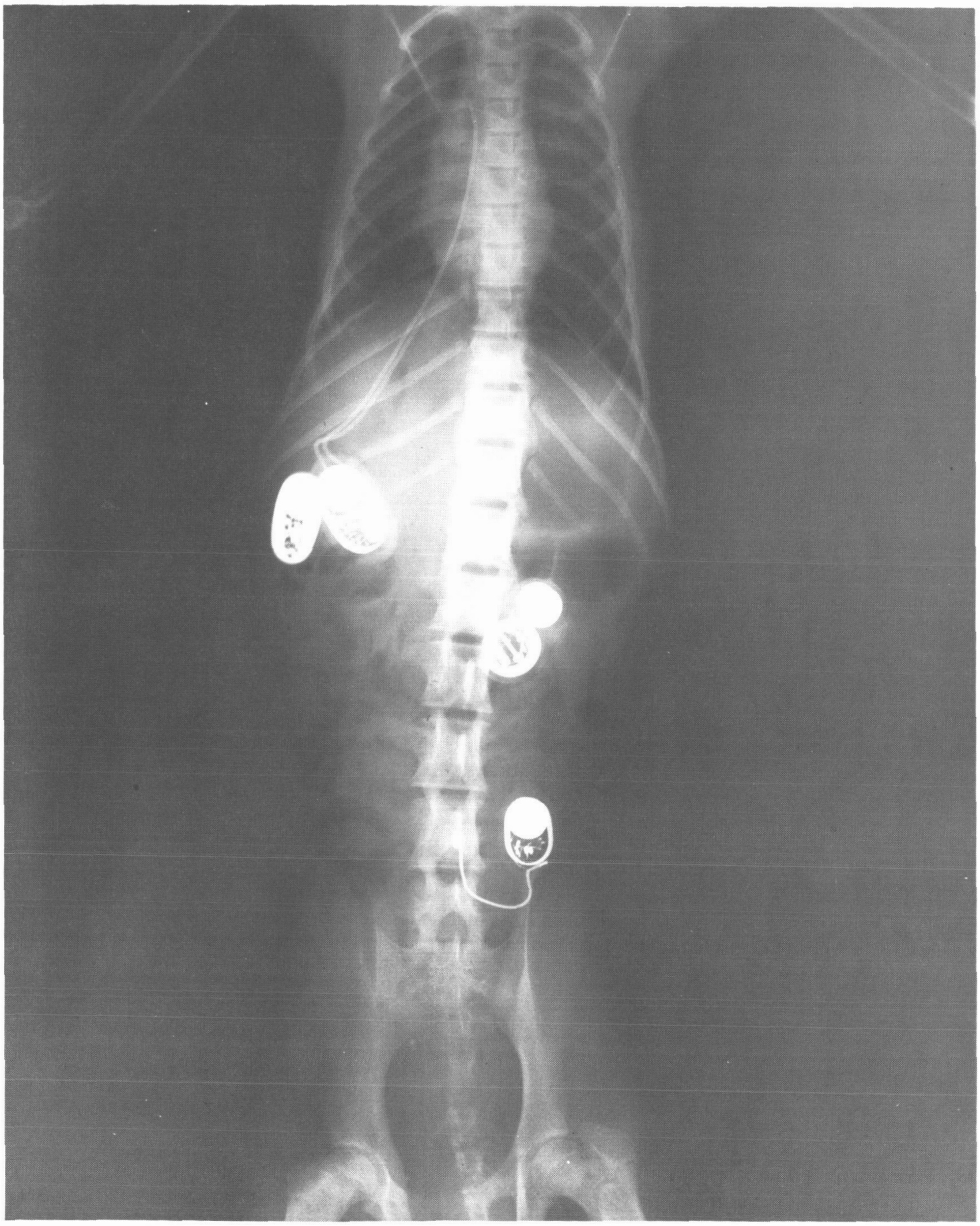


Fig. 11. X-ray image of Rhesus monkey with implanted transmitters of (from top to bottom) electrocardiogram, temperature, acceleration or motion, and blood pressure. For a given transmitter size, it is found that a stronger signal results from a small antenna coil beside the battery than from a larger coil encircling the battery.

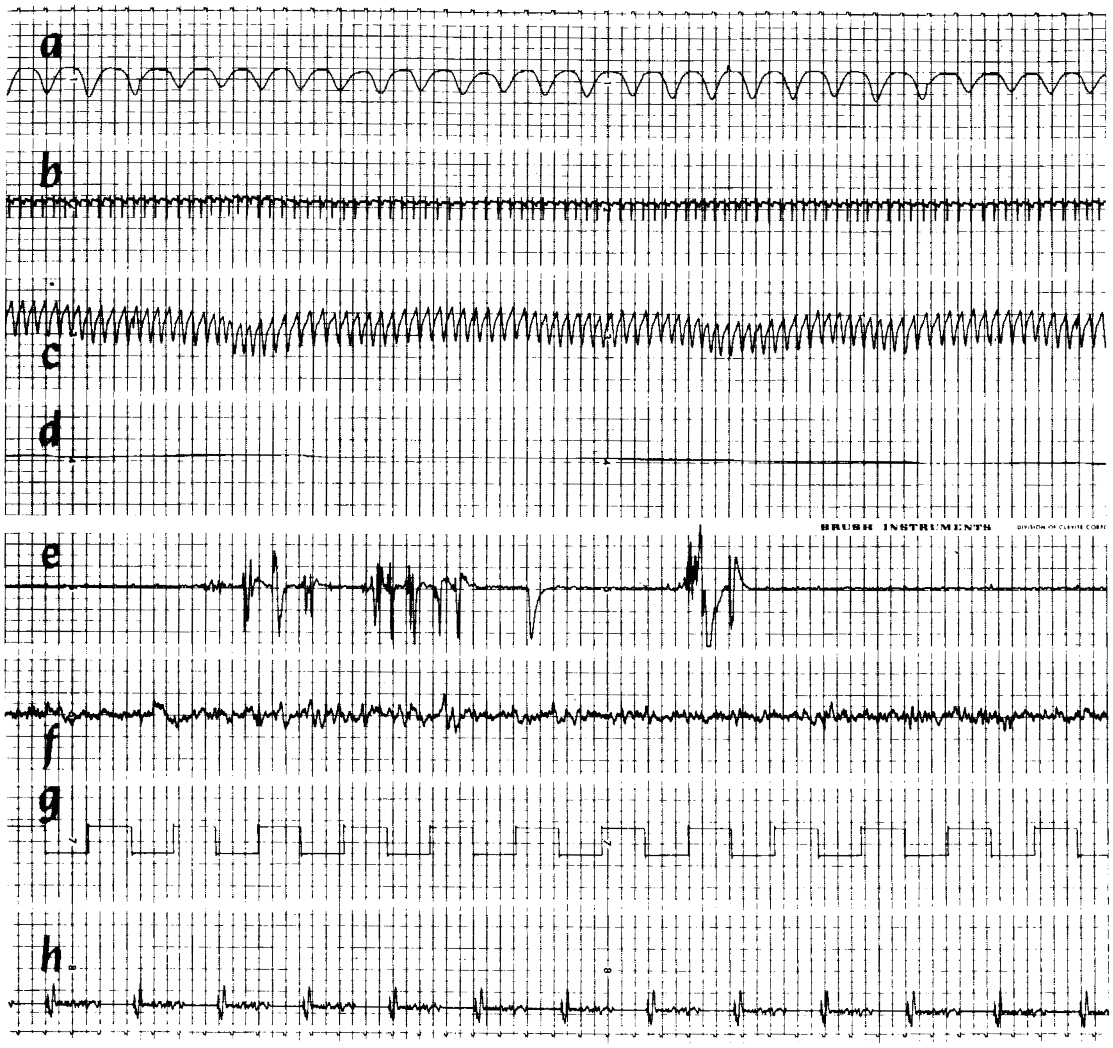


Fig. 12. Multiple transmissions of several variables simultaneously from within even a small animal such as a rabbit are possible. Here are simultaneous recordings of (a) respiration from pressure changes measured in the chest cavity; (b) electrocardiogram from leads and transmitter implanted under the skin; (c) blood pressure from intact wall of the abdominal aorta; (d) temperature in the abdominal cavity; (e) motion, from an accelerometer in cavity; (f) electrocorticogram from an active electrode over the optic cortex; (g) light flash marker - a brief flash accompanies each downstroke; (h) brain-wave response to light flash as simultaneously analyzed by an evoked response computer from the electrocorticogram. One-second time markers are at top and bottom. These signals were all received by an omnidirectional antenna consisting of three perpendicular coils wound on a ferrite sheet. The three outputs passed through frequency doublers before being added and passed to receivers used to decode the different frequency transmissions.

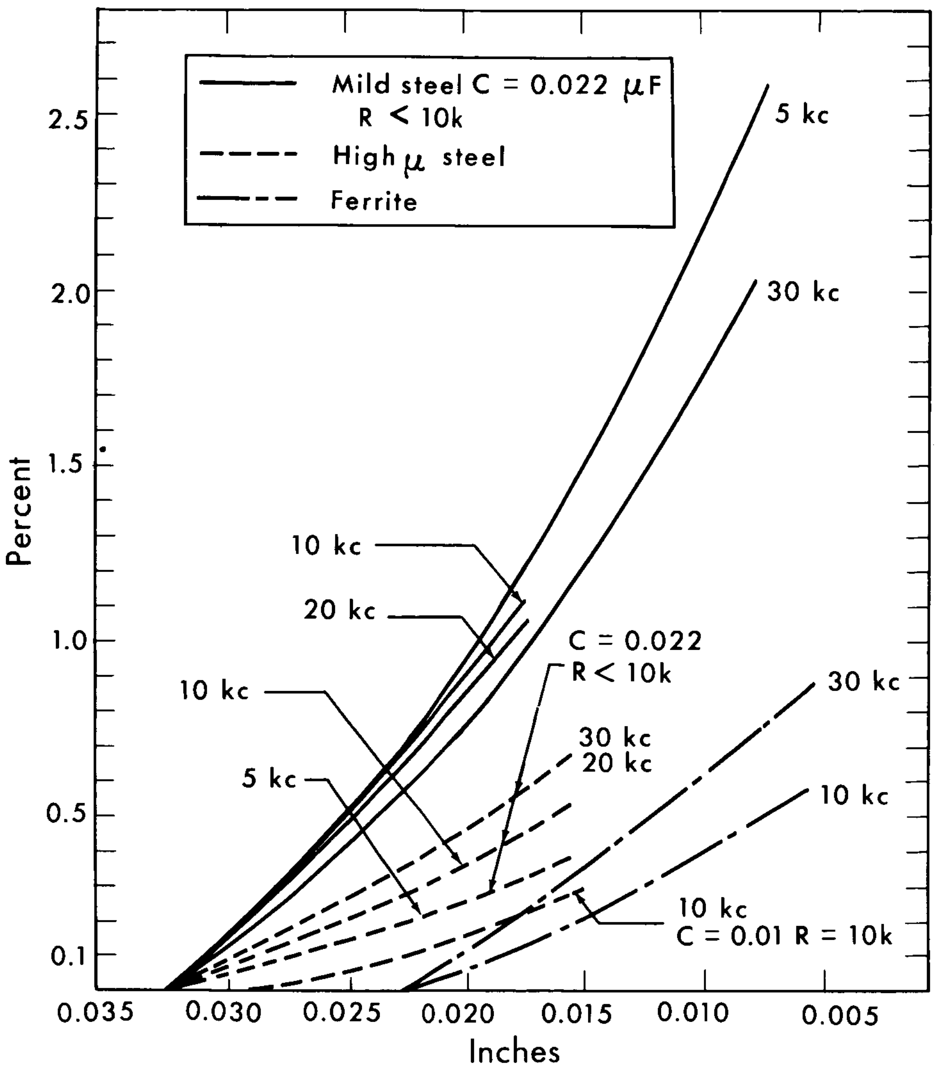


Fig. 13. The blocking version of Fig. 2 is pulse frequency modulated by motion of a ferromagnetic armature in response to pressure changes. The frequency sensitivity for several combinations is shown.

Fig. 14. Telemetering deep body temperature from within a 400 pound tortoise on the Galapagos Islands. The circuit of Fig. 2 was used with a two microfarad base condenser, thus giving a pulse rate that could be timed with a stop watch. Transmission through this thickness of tissue was strong to an unmodified pocket radio receiver seen resting on the shell of the animal.

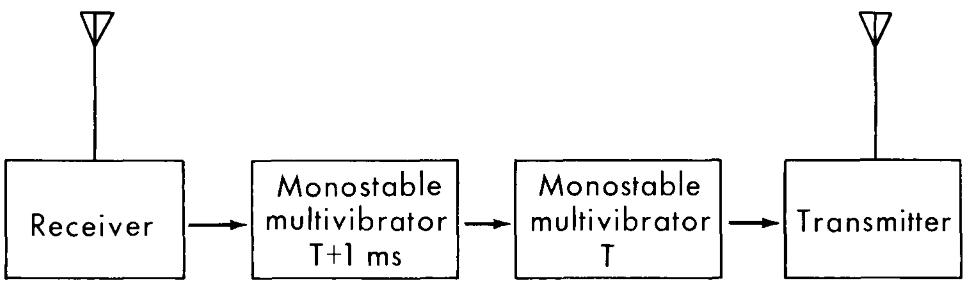


Fig. 15. Arrangement of booster retransmitter for use with endoradiosondes employing pulse frequency modulated transmission. Depending on receiver construction and the closeness of ingoing and outgoing frequencies, a single multivibrator may be sufficient. In this case, an omnidirectional receiver for strong signals may simply employ three coils feeding the input through any rectifier type. A booster transmitter for continuous oscillation signals must have a local oscillator to produce a frequency shift so that output will not affect input.

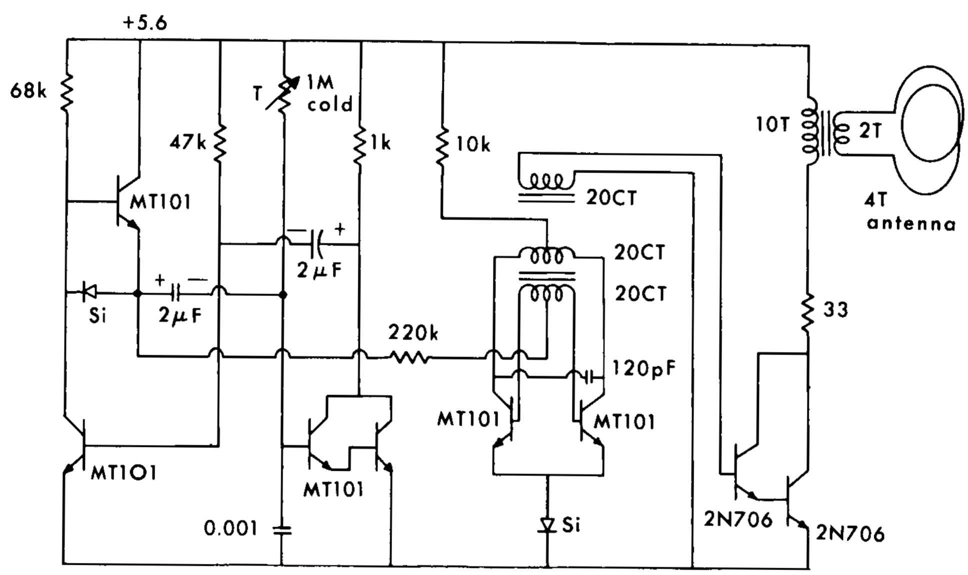
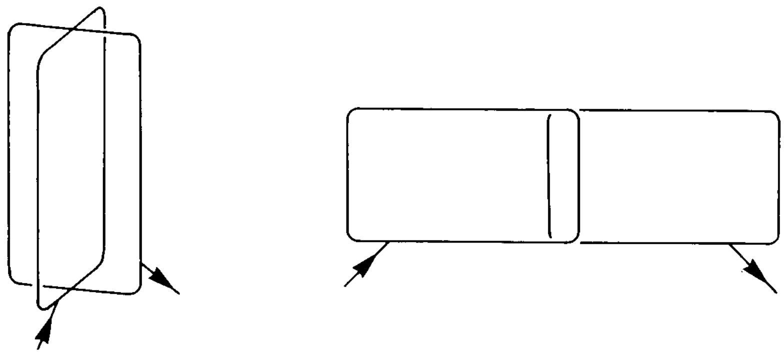


Fig. 16. Transmitter used to track and monitor body temperature of the Galapagos marine iguana at ranges of 100 feet. The multivibrator switches the transmitter on periodically at a rate that can be timed with a stop watch, and whose frequency is determined by temperature. Though small, this transmitter would normally be carried externally, with the thermistor in a probe. However, one can design partially soluble transmitters which, after being swallowed, would eventually fragment due to electrolytic action, and then the pieces spontaneously pass.



a.   b.

Fig. 17. Configurations of coil pairs providing no direct coupling between members: (a) coils perpendicular; (b) coils essentially in the same plane. A passive transmitter (LC tuned circuit with one member varying in response to some physiological variable) in the vicinity of such a system can carry energy between coils at its characteristic frequency. Thus it is found that an oscilloscope connected to one coil will show a maximum that contains the required information when an input radio frequency to the other coil is cyclically scanned up and down. If the energizing field is made uniform, signal strength falls off with the cube rather than sixth power of distance.

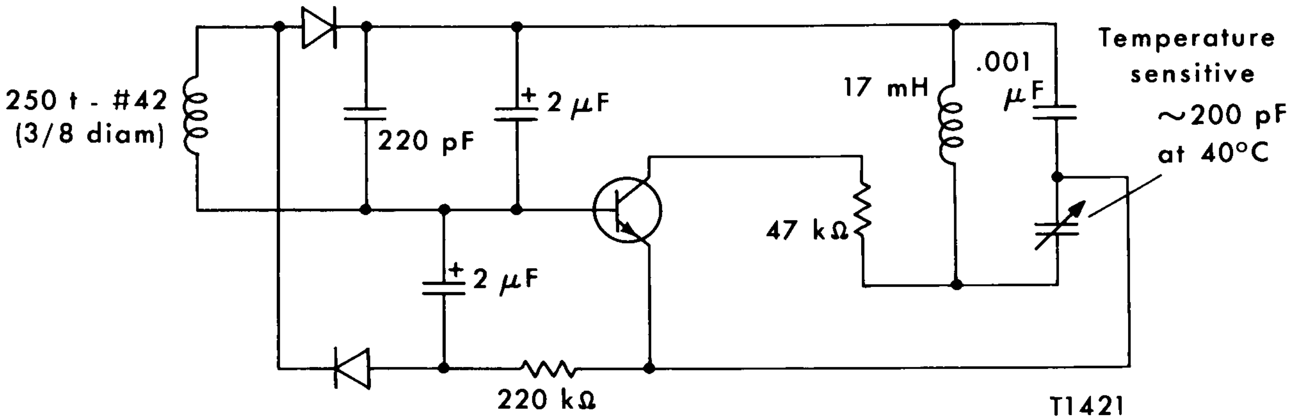


Fig. 18. Another type of transmitter that might be termed passive. This externally energized transmitter telemeters temperature, sensed as capacity variations. Power is induced into the full-wave voltage-doubler at one megacycle, and the signal reradiated at 100 kilocycles. The condenser must be chosen so that its dielectric shows no hysteresis in a temperature cycle.

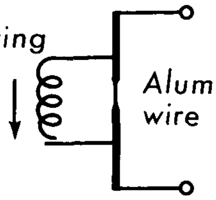


Fig. 19. A soluble transmitter perhaps is not feasible, but a large one which spontaneously fragments into small, readily passed pieces can be built around the above connection. The electrolytic action between the spring and wire eventually causes fragmentation when placed ina fluid such as gastric juice, and the time delay in some cases can be increased by placing a resistor in series with the spring. In general, transmitter size is limited by the antenna and perhaps the battery, rather than the electronic components; if a simple size change of inert components is all that is desired, solid gelatin projections on the capsule could be used. Such an arrangement might allow a large unit to remain in the stomach for a period, after which it could safely pass. Absorbable suture can be spring-loaded to tear a thin gold wire, after a delay, for similar purposes. The same system can be used to release medication, or to open and then close a sampling capsule after fixed times. Experiments may prove that simple solution of an iron wire with a permeable inert coating may similarly serve. A probe of intestinal size can similarly be constructed, with fragmentation upon external signal being effected by an external a.c. field demagnetizing and causing repulsion between "permanent magnets" holding the parts together.

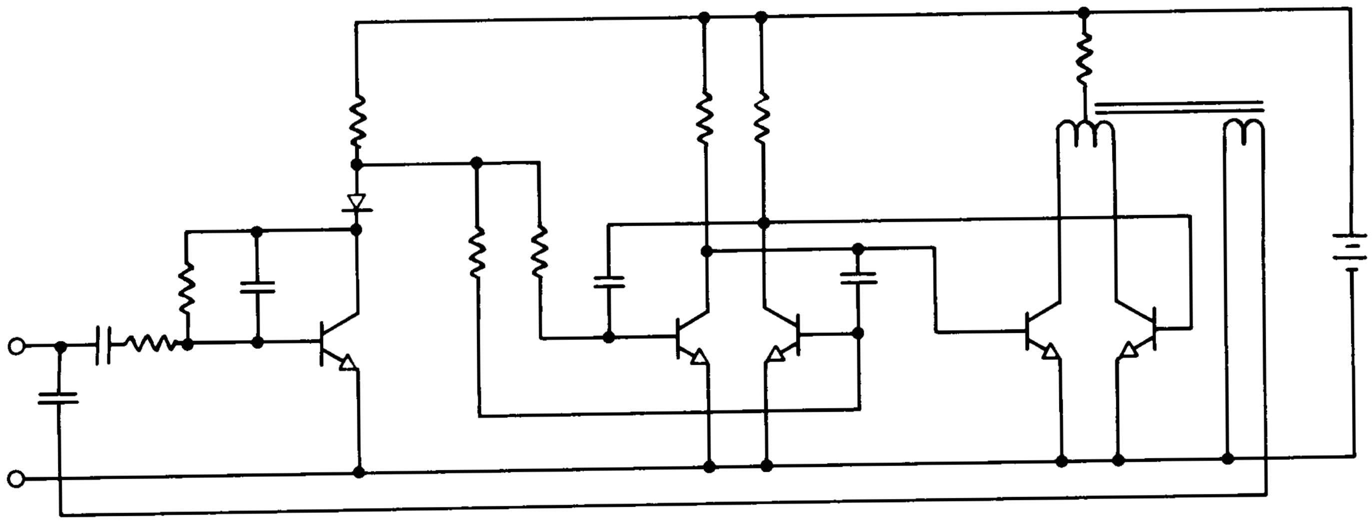


Fig. 20. Electrocardiogram transmitter which picks up the EKG voltage on a pair of electrodes and transmits the signal out through the same electrodes. Circuit constants are different for dolphin and human experiments. If swallowed, motion in the stomach can alter some aspects of the pattern.

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